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EFFECTS OF NITROGEN DIOXIDE ON PULMONARY FUNCTION IN HUMAN SUBJECTS

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Twenty human subjects with asthma and chronic bronchitis and ten normal, healthy adults were esposed to 0.5 ppm of nitrogen dioxide (NO_2) for two hours in an environmental chamber. They engaged in one 15-minute, light to medium-exercise stint on a bicycle ergometer during this period. The subjects with asthma experienced the greatest symptoms with exposure to NO_2, i.e., seven of thirteen noting slight burning of the eyes, slight headache, and chest tightness or labored breathing with exercise. One each of the subjects with chronic bronchitis and the healthy, normal group experienced slight nasal discharge. Significant changes from control values for the group as a whole with exposure to NO_2 were observed for the following pulmonary function tests: quasi-state compliance for the twenty subjects with asthma and chronic bronchitis as well as for the ten normal subjects, and functional residual capacity for the twenty subjects with asthma and chronic bronchitis. Subjects with asthma and chronic bronchitis as separate groups (n = 13 and 7 respectively) did not show any significant changes in pulmonary function with the NO_2 exposure, even though the group of thirteen subjects with asthma experienced the greatest symptoms.

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EFFECTS OF NITROGEN DIOXIDE ON PULMONARY FUNCTION IN HUMAN SUBJECTS

AN ENVIRONMENTAL CHAMBER STUDY

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FOREWORD

The many benefits of our modern, developing, industrial society are accompanied by certain hazards. Careful assessment of the relative risk of existing and new man-made environmental hazards is necessary for the establishment of sound regulatory policy. These regulations serve to enhance the quality of our environment in order to promote the public health and welfare and the productive capacity of our Nation's population.

The Health Effects Research Laboratory, Research Triangle Park, conducts a coordinated environmental health research program in toxicology, epidemiology, and clinical studies using human volunteer subjects. These studies address problems in air pollution, non-ionizing radiation, environmental carcinogenesis and the toxicology of pesticides as well as other chemical pollutants. The Laboratory develops and revises air quality criteria documents on pollutants for which national ambient air quality standards exist or are proposed, provides the data for registration of new pesticides or proposed suspension of those already in use, conducts research on hazardous and toxic materials, and is preparing the health basis for non-ionizing radiation standards. Direct support to the regulatory function of the Agency is provided in the form of expert testimony and preparation of affidavits as well as expert advice to the Administrator to assure the adequacy of health care and surveillance of persons having suffered imminent and substantial endangerment of their health.

This study was designed to look at the adverse effects, if any, of inhalation of NO_2 by human subjects with known diagnosis of asthma or chronic bronchitis. NO_2, at the levels studied, often is present in "smog" type atmospheres as are individuals with respiratory illness. This study gives some insight into the effect of a specific pollutant (NO_2) at a known concentration (.5 ppm) and time (2 hours) on an already compromised human respiratory system. Results from this investigation will provide data on the spectrum of pulmonary responses in two large classes of the population at risk. The data will aid HERL in further defining short-term adverse effects of this specific pollutant.

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Health Effects Research Laboratory

ABSTRACT

Twenty human subjects with asthma and chronic bronchitis and ten normal, healthy adults were exposed to 0.5 ppm of nitrogen dioxide (NO_2) for two hours in an environmental chamber. They engaged in one 15-minute, light to medium-exercise stint on a bicycle ergometer during this period. The subjects with asthma experienced the greatest symptoms with exposure to NO_2, i.e., seven of thirteen noting slight burning of the eyes, slight headache, and chest tightness or labored breathing with exercise. One each of the subjects with chronic bronchitis and the healthy, normal group experienced slight nasal discharge. Significant changes from control values for the group as a whole with exposure to NO_2 were observed for the following pulmonary function tests: quasi-state compliance for the twenty subjects with asthma and chronic bronchitis as well as for the ten normal subjects, and functional residual capacity for the twenty subjects with asthma and chronic bronchitis. Subjects with asthma and chronic bronchitis as separate groups (n = 13 and 7 respectively) did not show any significant changes in pulmonary function with the NO_2 exposure, even though the group of thirteen subjects with asthma experienced the greatest symptoms.

CONTENTS

		Page
Abstract		iv
List of Tables		vi
Acknowledgments		vii
Sections		
I	Conclusions	1
II	Recommendations	2
III	Introduction	3
IV	Materials and Methods	4
V	Experimental Phase (Results)	9
VI	Discussion	16
VII	References	17
VIII	Glossary	20

TABLES

No.		Page
1	Anthropometric Data, Smoking History, and Symptoms During Exposure to Nitrogen Dioxide of 30 Human Subjects Classified According to Diagnosis	11
2	Mean Values of Ventilatory Function Derived from Spirometry	12
3	Mean Values of Tests Derived from Plethysmographic Measurements	13
4	Mean Values of Tests Derived from Single-Breath N_2 Elimination Rate	14
5	Mean Values of Tests Derived from Measurements of Transpulmonary Pressure	15

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SECTION I

CONCLUSIONS

The symptoms reported were minimal, did not correlate with functional changes, and are of doubtful significance.

The results of this investigation are in general negative, which is in itself useful. It appears that no significant alteration in pulmonary function is likely to result from a two-hour exposure to 0.5 ppm NO_2 alone in normal subjects or patients with chronic obstructive pulmonary disease. The few significant changes reported here may be due to chance alone.

SECTION II

RECOMMENDATIONS

It is of interest to compare this NO_2 study with a previously reported 6-hour ozone exposure study with normal human subjects, also conducted in our environmental chamber, using the same 0.5 ppm concentration. With ozone (0.5 ppm for 6 hours), significant decrements in pulmonary function occurred with exposure for the 20 subject group as a whole in specific airway conductance, pulmonary resistance, forced vital capacity, and 3-second forced expiratory volume. However, no significant changes in specific airway conductance and forced vital capacity occurred following the first two-hours of ozone exposure; the changes reached significance only after four and six hours, respectively, of exposure. Subjects, who experienced symptoms, in general, were those who developed objective evidence of decreased pulmonary function.

With this study we are reasonably confident that exposure of patients with asthma and chronic bronchitis to 0.5 ppm NO_2 for two hours does not produce a significant decrement in pulmonary function. Exposure of 0.5 ppm NO_2 for longer than two hours could result in a significant decrement and possible correlation with the symptoms experienced with exposure.

Concern could be expressed for patients with COPD exposed to 0.5 ppm NO_2 for longer than two hours, i.e., six hours. Further studies using increased exposure time appear appropriate.

SECTION III

INTRODUCTION

Nitrogen dioxide (NO_2) levels in urban air pollution episodes in the U.S. (1962 - 1968) have been measured between 0.10 and 0.80 parts per million (ppm) as a maximum hourly average with short-term peaks as high as 1.27 ppm (1). The industrial hygiene occupational exposure for nitrogen dioxide is set by the American Conference of Government Industrial Hygienists (ACGIH) at 5 ppm as a ceiling value not to be exceeded (2). Limited studies of the toxic effects of NO_2 in man generally have considered high exposure levels (0.5 to 5.0 ppm) for periods of time from ten minutes to three hours. Measurements of pulmonary function have shown conflicting results; in some cases marked increase in pulmonary resistance was observed with exposure, while no change in pulmonary function was reported by other investigators (3, 4, 5). Epidemiologic and pulmonary function studies of children and their families living in neighborhoods with elevated NO_2 levels (proximity to large TNT plant) have demonstrated diminished pulmonary function ($FEV_{0.75}$) and/or an excess of lower respiratory illnesses (6, 7, 8). Horvath, et.al., exposed normal human subjects to 0.5 ppm NO_2 for two hours, observing no significant decrement in pulmonary function (9).

Few controlled studies employing specific NO_2 exposures have been performed on subjects with chronic pulmonary disease. The purpose of this investigation was to determine if measurable pulmonary function effects occur breathing 0.5 ppm (940 $\mu g/m^3$) nitrogen dioxide for two hours in

patients with asthma and chronic bronchitis and in normal subjects.

SECTION IV

MATERIALS AND METHODS

In order to restrict environmental effects to nitrogen dioxide, these experiments were carried out with subjects confined to an environmentally controlled chamber. A more detailed description of the environmental chamber facility is presented in a previously published paper (10). Temperature was maintained at 75 $\pm 1^{\circ}$ F with relative humidity 45 ±5%. All room air was exhausted to the outside, instead of recirculating it through the conditioning system, enabling precise control of nitrogen dioxide concentration during the exposure phase. A complete room air exchange occurred every 2.5 minutes. Air entering the 2.1 x 4.3 x 2.4 meter (7 x 14 x 8 foot) exposure room was passed through high-efficiency particulate absolute filters and activated carbon filters approaching class 100 cleanliness (<100 particles $\geq$0.5 μm/foot^3) or (<3534 particles $\geq$0.5 μm/m^3).

Nitrogen dioxide, in compressed gas cylinders of 6000 ppm concentration, was accurately metered into the exposure room of the chamber via the room air input diffuser. For the safety of the human subjects, the NO_2 concentration was monitored, recorded, and controlled continuously by two NO_2 analyzers, one employing the colorimetric method, the other the coulometric method. The colorimetric analyzer has good accuracy but a long response time (90% of full scale indication) of nine

minutes; whereas, the coulometric analyzer used had a response time within one-half a minute, but with somewhat less accuracy, thus being able to rapidly indicate changes in NO_2 concentration in the exposure room when they occurred. Prior to and following the NO_2 study, the two analyzers were checked for standardization with an accurate NO_2 source at the National Bureau of Standards (NBS), Gaithersburg, Maryland, using the Federal Register Method described in Code of Federal Regulations 40 CFR, Part 50.

In order to assure accurate setting of the NO_2 concentration for each exposure study, the colorimetric analyzer was calibrated in the laboratory prior to and on the day of the NO_2 exposure of each subject. An NBS calibrated NO_2 permeation tube in a temperature-controlled portable permeator was used as the calibrator for setting the span controls on the analyzer. In addition, the coulometric analyzer was also checked for standardization at NBS midway between the two-year study.

Prior to initiating the subject exposure studies, an NO_2 concentration profile was taken of the chamber exposure room at four- and six-foot levels above the chamber room, representing sitting and standing levels of the subject's mouth and nose. The range of concentrations varied between 0.47 and 0.52 ppm NO_2.

Nitrogen dioxide monitor strip chart recordings were made during

each subject exposure. Means and standard deviations were determined from three minute data points over the two-hour exposure period. The means of the various exposures ranged between 0.49 and 0.51 ppm, with the standard deviations ranging from 0.01 to 0.02 ppm.

Thirteen subjects with asthma, seven with chronic bronchitis, and ten normal, healthy subjects, were studied. Informed consent was obtained from each subject after the nature of the procedure had been fully explained. Smokers were asked to abstain for 24 hours prior to, and during the two days of the research. Twenty-three subjects were male and seven female. Each subject served as his own control. The order of subject study in pairs and the sequence of physiological tests was not varied.

A two-day study procedure was employed; on the first or control day the subjects remained in the exposure room for two hours breathing filtered clean air. On the second day, they breathed 0.50 ppm nitrogen dioxide for two hours at the same time of the day. Pulmonary function tests were performed in sequence (spirometry, plethysmography, and single breath nitrogen elimination rate) at the beginning and following the two hour chamber confinement on both day 1 and day 2. The remaining two physiological tests (pulmonary resistance and compliance) were done following the above tests only at the end of the two hour confinement on day 1 and day 2. Bicycle ergometer exercise at a light-to-moderate

work load of 60-100 watts, depending upon the subject's physical characteristics and tolerance, at 60 RPM for 15 minutes was performed during the first hour on both day 1 and day 2. All pulmonary function tests were performed in a seated position to insure comparability of lung volumes from the various tests. To assure technically satisfactory subject performance, the subjects repeatedly executed each test, except those requiring the esophageal balloon, during preliminary practice sessions and before confinement on both days.

Ventilatory function testing was performed as a single forced vital capacity (FVC) by standard technique employing a waterseal direct writing spirometer. All volumes were expressed in liters (L) at body temperature, pressure, saturated (BTPS).

Airway resistance (Raw) and volume of thoracic gas (Vtg) were determined by the whole-body pressure plethysmographic technique of DuBois, et.al. (11) with certain technical modifications (10). Each of ten panting breaths for Raw and Vtg at functional residual capacity (FRC) were determined by computer analysis of analog tape recordings of pressures, flow, and volume. Airway resistance measurements determined at 1 L/sec. airflow (0.5 L/sec. inspiratory to 0.5 L/sec. expiratory) were converted to specific airway conductance (SGaw = 1/Raw/Vtg), using the Vtg at which each Raw was measured, and expressed as the mean of the ten panting breaths. Practice sessions

enabled most subjects to perform the panting maneuvers of Raw and Vtg at or very close to FRC. Total lung capacity (TLC) was expressed as the sum of FRC and the inspiratory capacity, and residual volume (RV) was expressed as the difference between FRC and the expiratory reserve volume. All lung volumes were expressed in liters and SGaw as 1/cm H_2O x sec. units.

Tests of single breath nitrogen elimination rate were calculated from an XY plot of expired nitrogen concentration vs. expired volume from TLC to RV following a full inspiration of 100% oxygen from RV to TLC. Rate of expiration was controlled to not exceed 0.5 L/sec. Phase III was expressed as change in percent alveolar nitrogen concentration per liter of expired volume, and was determined from the best fit straight line of the alveolar sample mid-portion of the XY plot. Phase IV ("closing volume") was measured from RV to the Phase III-Phase IV junction (12). One reader performed all of the line-fitting procedures.

Pulmonary resistance (R_L) and compliance (C_L) were determined by the electronic subtractor method of Mead and Whittenberger (13). In order to stabilize volume history, each subject fully inflated his lungs to TLC prior to performing the quasi-static and dynamic compliance maneuvers. Dynamic compliance was performed at frequencies of 16 breaths per minute (C_L dyn. 16), 32/min. and 48/min. in rhythm with an audio

metronome while maintaining a tidal volume of one liter for 8 to 10 breaths at each breathing frequency. To determine C_L dyn., a portion of the transpulmonary pressure proportional to airflow was subtracted by manual potentiometer adjustment for the best fit straight line XY oscilloscope display of this resultant pressure vs. tidal volume. For R_L, a portion of transpulmonary pressure proportional to volume change was subtracted in a similar fashion with straight line fitting of the XY plot of this pressure vs. airflow. All subtractions and readings were performed from playback of analog tape recordings of airflow, volume change, and transpulmonary pressure. This procedure enabled re-reading of the recordings to verify values and also to standardize the length of time each subject performed at the different frequencies, thereby avoiding excessive alveolar ventilation from prolonged measurement. Pulmonary resistance was expressed as cm H_2O/L/sec. and was not corrected for the Vtg at which it was measured. All compliance data were expressed as ml/cm H_2O.

SECTION V

EXPERIMENTAL PHASE (RESULTS)

The odor of nitrogen dioxide was readily perceptible at the 0.50 ppm concentration, but most subjects reported that they became unaware of the odor after 15 minutes of exposure. None of the subjects considered the odor to be unpleasant. Subjects were asked to keep note of symptoms they might experience; following the exposure study, they were

specifically asked about cough, sputum, irritation of mucous membranes, and chest discomfort. Symptoms reported were in general mild and more frequently reported by subjects with asthma. Only one chronic bronchitis patient and one normal subject experienced the very mild symptom of slight rhinorrhea (Table 1), while more than half (seven of thirteen) asthma patients reported some degree of chest tightness, burning of the eyes, headache or dyspnea with exercise and exposure to NO_2. There did not appear to be any relationship between history and symptoms.

Although asthma patients experienced the most symptoms, no significant changes were observed in any of the parameters of pulmonary function (Tables 2 to 5). Normal subjects disclosed variance in the pre-exposure (0-Hour) Phase IV nitrogen elimination rate; but, there was no significant difference between the control and exposure (2-Hour) values (Table 4). After NO_2 exposure, a significant decrement in static compliance was noted in normal subjects but not observed in either patient group; while there were no significant changes in dynamic compliance for any subject group (Table 5). Chronic bronchitis patients demonstrated variance in the pre-exposure (0-Hour) Phase III nitrogen elimination rate, although no significant difference was shown between the control and exposure (2-Hour) values (Table 4). No other significant differences were observed in any of the pulmonary function tests. When the data for all twenty patients are considered together,

TABLE 1

ANTHROPOMETRIC DATA, SMOKING HISTORY, AND SYMPTOMS DURING EXPOSURE TO NITROGEN DIOXIDE OF 30 HUMAN SUBJECTS CLASSIFIED ACCORDING TO DIAGNOSIS

Subject No.	Sex	Age (years)	Height (cm)	Weight (kg)	Smoking History *	Symptoms During Exposure †
			Normal (n = 10)			
1	M	44	188	73	+	0
2	M	29	175	66	+	0
3	M	42	183	77	0	0
4	M	63	174	64	0	+ (nasal discharge)
5	M	39	173	70	0	0
6	M	26	183	70	0	0
7	M	28	190	92	0	0
10	M	29	183	83	+ (pipe)	0
11	M	22	179	79	0	0
12	M	23	190	83	0	0
Mean		34.5	181.8	75.7	3/10	1/10
S.D.		12.7	6.4	8.7		
			Chronic Bronchitis (n = 7)			
13	M	53	171	86	0	0
17	M	25	165	99	+ (pipe)	0
20	M	30	188	92	+	0
21	M	24	175	75	+	0
26	F	32	168	75	+	+ (nasal discharge)
29	F	24	168	61	0	0
30	F	24	161	76	+	0
Mean		30.3	170.8	80.6	3/7	1/7
S.D.		10.5	8.7	12.7		
			Asthma (n = 13)			
8	M	41	161	68	0	0
9	M	23	178	75	0 (former smoker)	0
14	M	30	165	64	+ (occasional)	+ (chest tightness)
15	M	22	164	65	0	+ (slight headache)
16	M	24	185	64	+	0
18	F	19	159	62	0	+ (slight burning of eyes)
19	F	21	166	62	0	0
22	M	21	173	68	0	0
23	F	38	160	49	0	+ (chest tightness)
24	M	50	175	80	0 (former smoker)	+ (chest tightness)
25	M	20	175	72	0	+ (slight burning of eyes)
27	M	20	185	69	+ (light)	+ (dyspnea with exercise)
28	F	19	171	73	0	0
Mean		26.8	170.5	67.0	3/13	7/13
S.D.		10.0	8.9	7.6		

* 0, nonsmoker; +, smoker

† 0, no symptoms; +, symptom experienced.

TABLE 2

MEAN VALUES OF VENTILATORY FUNCTION DERIVED FROM SPIROMETRY

Subject Groups	Normal Subjects (n = 10)			Patients with Asthma (n = 13)			Patients with Chronic Bronchitis (n = 7)		
	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means
	Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)	
FVC									
0-Hour	[illegible]5	[illegible].29	0.05	4.51	4.49	0.07	4.88	4.93	0.04
2-Hour	[illegible].30	[illegible].27	0.03	4.42	4.38	0.05	4.81	4.82	0.06
FEV 1									
0-Hour	4.05	4.06	0.05	3.15	3.25	0.07	3.66	3.64	0.04
2-Hour	4.14	4.10	0.04	3.12	3.14	0.05	3.50	3.51	0.08
FEV 3									
0-Hour	4.91	4.98	0.05	4.15	4.18	0.06	4.47	4.51	0.03
2-Hour	4.98	4.94	0.03	4.09	4.07	0.05	4.38	4.38	0.06
MEFR									
0-Hour	9.79	9.04	0.54	5.76	5.85	0.27	8.14	8.07	0.61
2-Hour	10.00	9.55	0.42	5.93	5.86	0.30	7.20	7.51	0.47
MMEF									
0-Hour	3.70	3.69	0.10	2.51	2.83	0.18	3.15	3.02	0.12
2-Hour	3.94	3.74	0.13	2.65	2.70	0.13	2.71	2.81	0.23
ERV									
0-Hour	1.84	1.81	0.10	1.37	1.23	0.08	1.63	1.63	0.08
2-Hour	1.82	1.67	0.08	1.25	1.24	0.04	1.55	1.53	0.07

TABLE 3

MEAN VALUES OF TESTS DERIVED FROM PLETHYSMOGRAPHIC MEASUREMENTS

Subject Groups	Normal Subjects (n = 10)			Patients with Asthma (n = 13)			Patients with Chronic Bronchitis (n = 7)			All Patients (n = 20)		
	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means
	Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)	
SGaw												
0-Hour	.218	.219	.014	.137	.136	.007	.196	.185	.016	.158	.153	0.007
2-Hour	.246	.238	.014	.137	.142	.012	.198	.180	.014	.159	.156	0.009
TLC												
0-Hour	7.24	7.37	0.13	6.47	6.65	0.11	6.67	6.87	0.11	6.54	6.74†	0.08
2-Hour	7.38	7.44	0.17	6.32	6.49	0.11	6.63	6.86	0.13	6.44	6.63*	0.08
FRC												
0-Hour	3.83	3.90	0.10	3.37	3.40	0.09	3.42	3.57	0.09	3.39	3.46	0.07
2-Hour	3.91	3.83	0.13	3.19	3.38	0.13	3.37	3.57	0.13	3.26	3.45*	0.09
RV												
0-Hour	1.99	2.08	0.12	1.96	2.16	0.09	1.79	1.94	0.08	1.90	2.08†	0.07
2-Hour	2.08	2.16	0.18	1.90	2.11	0.12	1.82	2.04	0.11	1.87	2.09†	0.09

*$p < .05$

†$p < .025$

TABLE 4

MEAN VALUES OF TESTS DERIVED FROM SINGLE-BREATH N_2 ELIMINATION RATE

Subject Groups	Normal Subjects (n = 10)			Patients with Asthma (n = 13)			Patients with Chronic Bronchitis (n = 7)			All Patients (n = 20)		
	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means
	Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)	
Phase III												
0-Hour	1.15	1.26	0.13	1.42	1.58	0.18	1.14	0.85†	0.07	1.32	1.33	0.13
2-Hour	1.13	1.08	0.13	1.30	1.41	0.11	1.15	0.92	0.10	1.28	1.22	0.07
Phase IV												
0-Hour	0.62	0.47*	0.06	0.44	0.35	0.06	0.41	0.53	0.13	0.43	0.41	0.06
2-Hour	0.54	0.65	0.07	0.36	0.39	0.06	0.48	0.39	0.18	0.41	0.39	0.07
Phase IV + RV												
0-Hour	2.61	2.55	0.14	2.44	2.54	0.09	2.20	2.47	0.15	2.35	2.51	0.08
2-Hour	2.62	2.81	0.20	2.30	2.54	0.13	2.30	2.43	0.18	2.30	2.50	0.10

*$p < .05$

†$p < .01$

TABLE 5

MEAN VALUES OF TESTS DERIVED FROM MEASUREMENTS OF TRANSPULMONARY PRESSURE

Subject Groups	Normal Subjects (n = 10)			Patients with Asthma (n = 13)			Patients with Chronic Bronchitis (n = 7)			All Patients (n = 20)		
	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means	Mean		Standard Error of Difference in Means
	Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)		Day 1 (Control)	Day 2 (Exposure)	
R_L 2-Hour	2.00	1.94	0.10	4.41	4.43	0.19	3.23	3.17	0.11	4.00	3.99	0.13
C_L Stat 2-Hour	346	286*	18	269	253	10	366	334	18	303	282†	9
C_L dyn 16 2-Hour	196	197	12	160	159	6	210	207	9	178	176	5
C_L dyn 32 2-Hour	190	189	18	137	131	7	187	193	14	153	150	7
C_L dyn 48 2-Hour	194	194	21	121	123	7	155	170	8	133	140	6

*$p < .025$
†$p < .05$

significant increases were noted in TLC, FRC, RV, and static compliance on the exposure day (Tables 3 and 5).

SECTION VI

DISCUSSION

A double-blind study would have been desirable for this research. However, the odor of NO_2 is detectable at 0.5 ppm, thus making a double-blind study impractical. The symptoms reported in this study were in general mild and more frequently reported by the subjects with asthma. Although these patients experienced the most symptoms no significant changes in pulmonary function were observed.

Considering the 13 patients with asthma and the seven patients with chronic bronchitis, significant changes in some pulmonary function parameters only occurred when they were grouped together as 20 subjects. These changes in compliance, distribution of ventilation and static lung volumes (TLC, FRC, RV) suggest some degree of change in elastic properties. However, no meaningful change in function can be implied as significant differences also were generally observed prior to exposure. There were no significant changes in any of the flow resistance parameters by spirometry, plethysmography, or esophageal balloon techniques.

SECTION VII

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SECTION VIII

GLOSSARY

Plethysmography - Body box method for determining airway resistance and static lung volumes.

Single Breath Nitrogen Elimination Rate - Percentage rise in nitrogen fraction per unit of volume expired.

Pulmonary Resistance (R_L) - The sum of airway resistance and viscous tissue resistance.

Static Compliance ($C_{L\ stat}$) - Measure of elastic recoil with no or insignificant airflow.

Dynamic Compliance ($C_{L\ dyn}$) - Volume change per unit of trans-pulmonary pressure minus the pressure of pulmonary resistance during airflow.